

FIG. 1

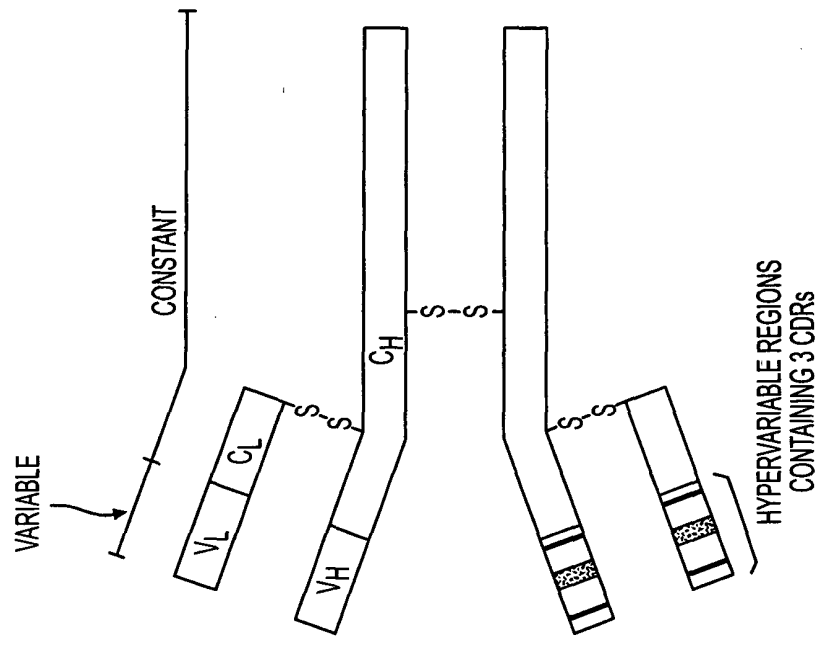


FIG. 2

EFFECT OF ANTI-STAPH MAB 96-110 ON
SURVIVAL IN A LETHAL S. AUREUS SEPSIS MODEL

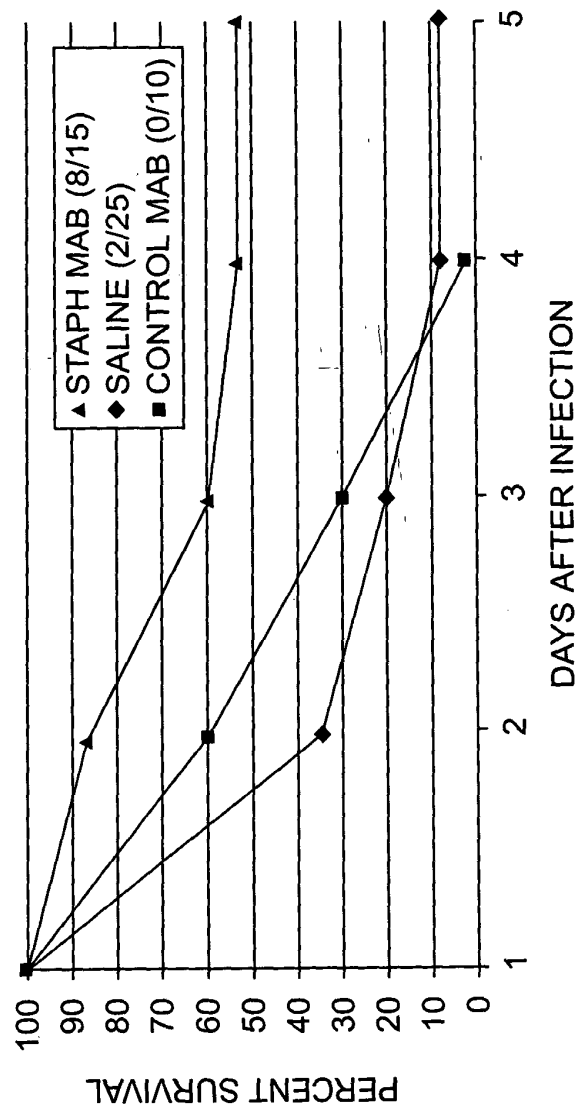


FIG. 3

PERCENT SURVIVAL OF CF-1 MICE
CHALLENGE WITH 3.5×10^9 S. HAY

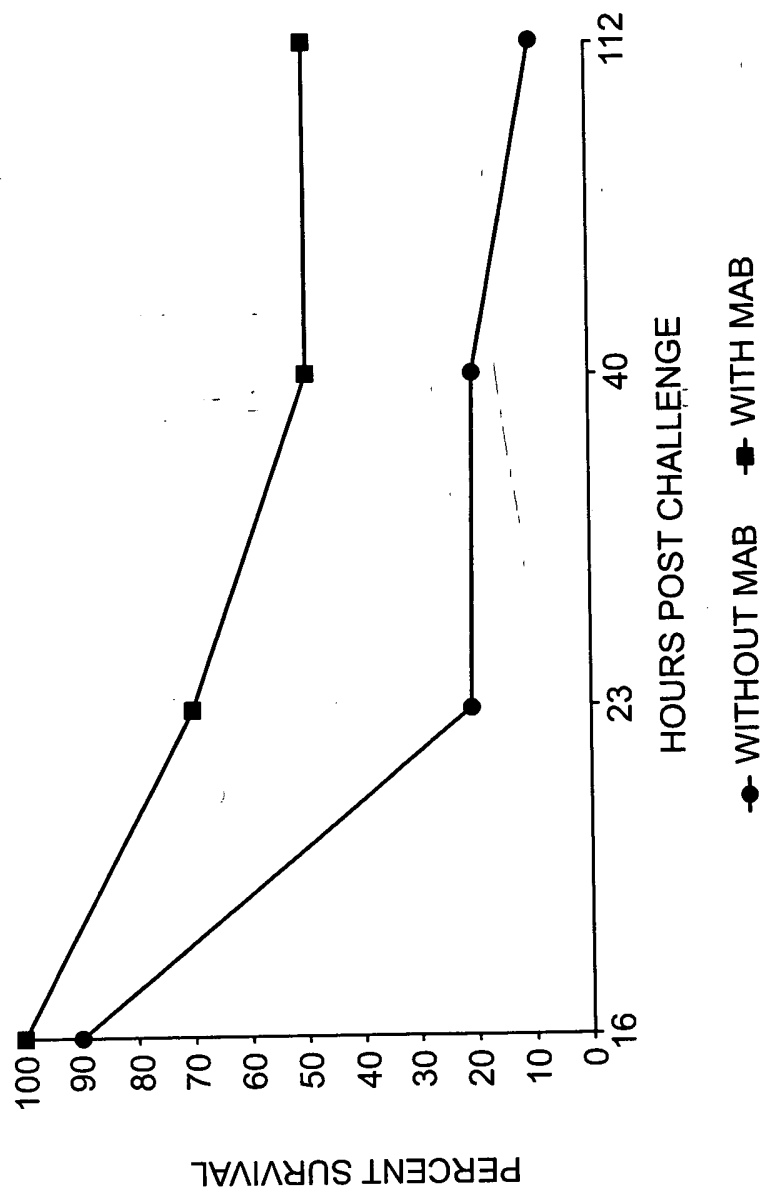


FIG. 4

6MER.SEQ

	10	20	30	
41:13.6mer2-1	GGGGCTCATG	CGGATAGGGT	TTATGGGGCC	SEQ ID NO.4
61	G A H	A D R V	Y G A	SEQ ID NO.5
42:14.6mer2-2	GGGGCTCATG	CGGATAGGGT	TTATGGGGCC	
65	G A H	A D R V	Y G A	
43:15.6mer2-3	GGGGCTCATG	CGGATAGGGT	TTATGGGGCC	
66	G A H	A D R V	Y G A	
44:16.6mer2-4	GGGA-TCATG	CGGATAGGGT	TTATGGGGCC	SEQ ID NO.6
62	G ? H	A D R V	Y G A	SEQ ID NO.7
45:17.6mer2-5	GGGGCTCATG	CGGATAGGGT	TTATGGGGCC	
67	G A H	A D R V	Y G A	
46:18.6mer2-6	GGGGCTCATG	CGGATAGGGT	TTATGGGGCC	
68	G A H	A D R V	Y G A	
47:19.6mer2-7	GGGGCTCATG	CGGATAGGGT	TTATGGGGCC	
69	G A H	A D R V	Y G A	
48:20.6mer2-8	GGGGCTCATG	CGGATAGGGT	TTATGGGGCC	
70	G A H	A D R V	Y G A	
49:21.6mer2-9	GGGGCTCATG	CGGATAGGGT	TTATGGGGCC	
71	G A H	A D R V	Y G A	
51:23.6mer2-11	GGGGCTCATG	CGGATAGGGT	TTATGGGGCC	
72	G A H	A D R V	Y G A	
52:24.6mer2-12	GGGGCTCATG	CGGATAGGGT	TTATGGGGCC	
73	G A H	A D R V	Y G A	
53:25.6mer2-13	GGGGCTCATG	CGGATAGGGT	TTATGGGGCC	
74	G A H	A D R V	Y G A	
54:26.6mer2-14	GGGGCTCATG	CGGATAGGGT	TTATGGGGCC	
75	G A H	A D R V	Y G A	
55:27.6mer2-15	GGGGCTCATG	CGGATAGGGT	TTATGGGGCC	
76	G A H	A D R V	Y G A	
56:28.6mer2-16	GGGGCTCATG	CGGATAGGGT	TTATGGGGCC	
77	G A H	A D R V	Y G A	
58:30.6mer2-18	GGGGCTCATG	CGGATAGGGT	TTATGGGGCC	
78	G A H	A D R V	Y G A	
59:31.6mer2-19	GGGGCTCATG	CGGATAGGGT	TTATGGGGCC	
79	G A H	A D R V	Y G A	
60:32.6mer2-20	GGGGCTCATG	CGGATAGGGT	TTATGGGGCC	
80	G A H	A D R V	Y G A	

FIG. 5

15MER2.SEQ

	10	20	30	40	50	60	
50:07.15mer2-1/0	GGGGCTTGGC	ATTGGCGTCA	TCGTATTCCT	CTTCAGCTTG	CTGCTGGTCG	TGGGGCC	SEQ ID NO. 8
70	G A (W)	H W R H	R I P	L O L	A A G	G A	SEQ ID NO. 9
52:09.15mer2-3/0	GGGGCTCGTC	GGCATGGTAA	TTTTTCTCAT	TTTTTTCATC	GGTCGTTGAT	TGGGGCC	SEQ ID NO. 10
72	G A R	(R) (H) G N	(F) (S) (H)	F F (H)	(R) S L I	G A	SEQ ID NO. 11
53:10.15mer2-4/0	GGGGCTTGA	AGGCTTGT	TATCATCT	TATCGTCTC	GGGTTGCGC	TGGGGCC	SEQ ID NO. 12
73	G A (W)	(K) A L (E)	(S) (H) S	Y (R) P	R G S A	G A	SEQ ID NO. 13
54:11.15mer2-5/0	GGGGCTAGGC	ATTGGCGTCA	TCGTATTCCT	CTTCAGCTTG	CTGCTGGTCG	TGGGGCC	SEQ ID NO. 14
74	G A R	H W R H	R I P	L O L	A A G	G A	SEQ ID NO. 15
56:13.15mer2-7/0	GGGGCTTGGC	ATTGGCGTCA	TCGTATTCCT	CTTCAGCTTG	CTGCTGGTCG	TGGGGCC	SEQ ID NO. 16
76	G A W	H W R H	R I P	L O L	A A G	G A	SEQ ID NO. 17
57:14.15mer2-8/0	GGGGCTTGGC	ATTGGCGTCA	TCGTATTCCT	CTTCAGCTTG	CTGCTGGTCG	TGGGGCC	SEQ ID NO. 18
77	G A W	H W R H	R I P	L O L	A A G	G A	SEQ ID NO. 19
58:15.15mer2-9/0	GGGGCTCAGG	TGGCTGTTT	GTATCCTCCT	TTGGCTGATG	CTACTGAGCT	TGGGGCC	SEQ ID NO. 20
78	G A Q	V A V L	Y P P	L A D	A T E L	G A	SEQ ID NO. 21
59:16.15mer2-10/0	GGGGCTCGTC	GGCATGGTAA	TTTTTCTCAT	TTTTTTCATC	GGTCGTTGAT	TGGGGCC	SEQ ID NO. 22
79	G A R	R H G N	F S H	F F H	R S L I	G A	SEQ ID NO. 23
60:17.15mer2-11/0	GGGGCTCGTC	GGCATGGTAA	TTTTTCTCAT	TTTTTTCATC	GGTCGTTGAT	TGGGGCC	SEQ ID NO. 24
80	G A R	R H G N	F S H	F F H	R S L I	G A	SEQ ID NO. 25
61:18.15mer2-12/0	GGGGCTTGGC	GTATGATTT	TTCTCATCGT	CATGCGCATC	TTGCTAGTCC	TGGGGCC	SEQ ID NO. 26
81	G A (W)	R M Y (E)	(S) (H) R	(H) A H	(L) R S P	G A	SEQ ID NO. 27
62:19.15mer2-13/0	GGGGCTTGGC	GTATGATTT	TTCTCATCGT	CATGCGCATC	TTGCTAGTCC	TGGGGCC	SEQ ID NO. 28
82	G A W	R M Y F	S H R	H A H	L R S P	G A	SEQ ID NO. 29
63:20.15mer2-14/0	GGGGCTTGGC	GGAAGTATTT	TTCTTATCAT	CATGCGCATC	TTTGTAGTCC	TGGGGCC	SEQ ID NO. 30
83	G A W	R K Y F	S Y H	H A H	L C S P	G A	SEQ ID NO. 31
54:21.15mer2-15/0	GGGGCTTGGC	GTATGATTT	TTCTCATCGT	CATGCGCATC	TTGCTAGTCC	TGGGGCC	SEQ ID NO. 32
84	G A W	R M Y F	S H R	H A H	L R S P	G A	SEQ ID NO. 33
55:22.15mer2-16/0	GGGGCTTGGC	GTATGATTT	TTCTCATCGT	CATGCGCATC	TTGCTAGTCC	TGGGGCC	SEQ ID NO. 34
85	G A W	R M Y F	S H R	H A H	L R S P	G A	SEQ ID NO. 35
56:23.15mer2-17/0	GGGGCTTGGC	GTATGATTT	TTCTCATCGT	CATGCGCATC	TTGCTAGTCC	TGGGGCC	SEQ ID NO. 36
86	G A W	R M Y F	S H R	H A H	L R S P	G A	SEQ ID NO. 37
57:24.15mer2-18/0	GGGGCTCGTC	GGCATGGTAA	TTTTTCTCAT	TTTTTTCATC	GGTCGTTGAT	TGGGGCC	SEQ ID NO. 38
87	G A R	R H G N	F S H	F F H	R S L I	G A	SEQ ID NO. 39
58:25.15mer2-19/0	GGGGCTTGGC	ATTGGCGTCA	TCGTATTCCT	CTTCAGCTTG	CTGCTGGTCG	TGGGGCC	SEQ ID NO. 40
88	G A W	H W R H	R I P	L O L	A A G	G A	SEQ ID NO. 41
59:26.15mer2-20/0	GGGGCTCGTC	GGCATGGTAA	TTTTTCTCAT	TTTTTTCATC	GGTCGTTGAT	TGGGGCC	SEQ ID NO. 42
89	G A R	R H G N	F S H	F F H	R S L I	G A	SEQ ID NO. 43

FIG. 6

15MER1.SEQ

	10	20	30	40	50	60	
51:28.15mer1-2/0	GGGGCTGATT	GGATTACTTT	TCATCGTCGT	CATCATGATC	GTGTTCTTTC	TGGGGCC	SEQ ID NO.44
67	G A D	(W) I T (F)	(H) R R	H (H) D	(R) V L S	G A	SEQ ID NO.45
52:29.15mer1-3/0	GGGGCTGGTT	GGATTACTTT	TCATCGTCGT	CATCATGATC	GTGTTCTTTC	TGGGGCC	SEQ ID NO.46
68	G A G	W I T F	H R R	H H D	R V L S	G A	SEQ ID NO.47
53:32.15mer1-6/0	GGGGCTGGTT	GGATTACTTT	TCATCGTCGT	CATCATGATC	GTGTTCTTTC	TGGGGCC	
65	G A G	W I T F	H R R	H H D	R V L S	G A	
62:13.15mer1-7/0	GGGGCTGGTT	GGATTACTTT	TCATCGTCGT	CATCATGATC	GTGTTCTTTC	TGGGGCC	
66	G A G	W I T F	H R R	H H D	R V L S	G A	
63:14.14mer1-8/0	GGGGCTGGTT	GGATTACTTT	TCATCGTCGT	CATCATGATC	GTGTTCTTTC	TGGGGCC	
67	G A G	W I T F	H R R	H H D	R V L S	G A	
64:15.15mer1-9/0	GGGGCTGGTT	GGATTACTTT	TCATCGTCGT	CATCATGATC	GTGTTCTTTC	TGGGGCC	
68	G A G	W I T F	H R R	H H D	R V L S	G A	
65:16.15mer1-10/0	GGGGCTGGTT	GGATTACTTT	TCATCGTCGT	CATCATGATC	GTGTTCTTTC	TGGGGCC	
69	G A G	W I T F	H R R	H H D	R V L S	G A	
56:17.15mer1-11/0	GGGGCTGGTT	GGATTACTTT	TCATCGTCGT	CATCATGATC	GTGTTCTTTC	TGGGGCC	
70	G A G	W I T F	H R R	H H D	R V L S	G A	
57:20.15mer1-12/0	GGGGCTGGTT	GGATTACTTT	TCATCGTCGT	CATCATGATC	GTGTTCTTTC	TGGGGCC	
71	G A G	W I T F	H R R	H H D	R V L S	G A	
58:29.15mer1-13/0	GGGGCTGGTT	GGATTACTTT	TCATCGTCGT	CATCATGATC	GTGTTCTTTC	TGGGGCC	
72	G A G	W I T F	H R R	H H D	R V L S	G A	
59:20.15mer1-14/0	GGGGCTGGTT	GGATTACTTT	TCATCGTCGT	CATCATGATC	GTGTTCTTTC	TGGGGCC	
73	G A G	W I T F	H R R	H H D	R V L S	G A	
70:21.15mer1-15/0	GGGGCTGGTT	GGATTACTTT	TCATCGTCGT	CATCATGATC	GTGTTCTTTC	TGGGGCC	
74	G A G	W I T F	H R R	H H D	R V L S	G A	
71:22.15mer1-16/0	GGGGCTGGGA	AGGCTATGTT	TACTCATTTCT	TATCGTCATC	GGGGTTCGGC	TGGGGCC	SEQ ID NO.48
75	G A G	(K) A M (F)	(S) H S	Y R (H)	(R) G S A	G A	SEQ ID NO.49
72:23.15mer1-17/0	GGGGCTGGTT	GGATTACTTT	TCATCGTCGT	CATCATGATC	GTGTTCTTTC	TGGGGCC	
76	G A G	W I T F	H R R	H H D	R V L S	G A	
73:24.15mer1-18/0	GGGGCTGGTT	GGATTACTTT	TCATCGTCGT	CATCATGATC	GTGTTCTTTC	TGGGGCC	
77	G A G	W I T F	H R R	H H D	R V L S	G A	
74:25.15mer1-19/0	GGGGCTGGTT	GGATTACTTT	TCATCGTCGT	CATCATGATC	GTGTTCTTTC	TGGGGCC	
78	G A G	W I T F	H R R	H H D	R V L S	G A	
75:26.15mer1-20/0	GGGGCTGGTT	GGATTACTTT	TCATCGTCGT	CATCATGATC	GTGTTCTTTC	TGGGGCC	
79	G A G	W I T F	H R R	H H D	R V L S	G A	

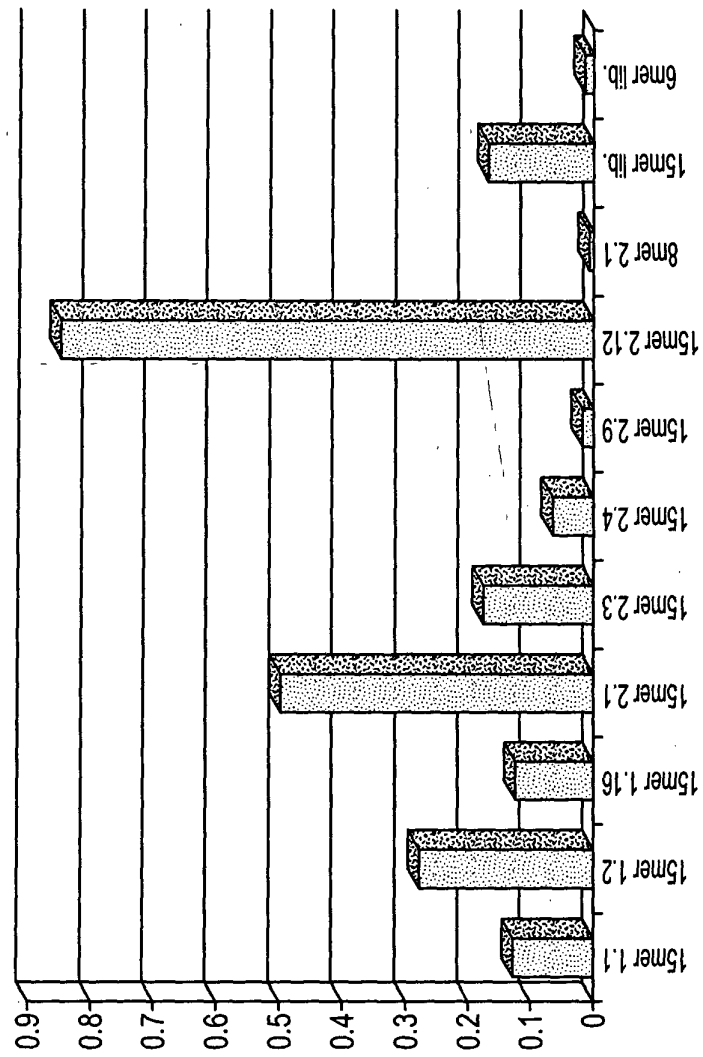
FIG. 7

MASTERLIST

	10	20	30	40	50	60	70
51: 15mer 1st.1	GGGGCTGATT	GGATTACTTT	TCATCGTCGT	CATCATGATC	GTGTTCTTTC	TGGGGCC	16/17 SEQ ID NO. 50
57	G A D W I T F	H R R H H D R V L S	TCGCGTTGG	TCGCGTTGC	TTGCTGTTCC	TGGGGCC	1/17 SEQ ID NO. 51
90 15mer 1st.7	GGGGCTAGTC	GTCATATGCT	TGCTCGGTGG	TCGCGTTTGC	TTGCTGTTCC	TGGGGCC	1/10 SEQ ID NO. 52
91	G A S R H M L	A R W S R L L A V P	TATCGTCATC	GGGTTTCGGC	TGGGGCC	1/10 SEQ ID NO. 53	
71: 15mer 1st.16	GGGGCTGGGA	AGGCTATGTT	TATCGTCATC	GGGTTTCGGC	TGGGGCC	1/17 SEQ ID NO. 54	
85	G A G K A M F	S H S Y R H R G S A	CTTCAGCTTG	CTGCTGGTCG	TGGGGCC	5/17 SEQ ID NO. 55	
92: 15mer 2nd.1	GGGGCTTGGC	ATTGGCGTCA	TCGTATTCCT	CTTCAGCTTG	CTGCTGGTCG	TGGGGCC	5/18 SEQ ID NO. 56
98	G A W H W R H	R I P L Q L A A G R	TTTTTTCATC	GGTCGTTGAT	TGGGGCC	6/18 SEQ ID NO. 57	
93 15mer 2nd.3	GGGGCTCGTC	GSCATGGTAA	TTTTTTCATC	GGTCGTTGAT	TGGGGCC	6/18 SEQ ID NO. 58	
99	G A R R H G N	F S H F F H R S L I	TATCGTCCTC	GGGTTTCGGC	TGGGGCC	1/18 SEQ ID NO. 59	
94: 15mer 2nd.4	GGGGCTTGA	AGGCTTTGTT	TATCGTCCTC	GGGTTTCGGC	TGGGGCC	1/18 SEQ ID NO. 60	
100	G A W K A L F	S H S Y R P R G S A	CTACTGAGCT	TGGGGCC	1/18 SEQ ID NO. 61		
95: 15mer 2nd.9	GGGGCTCAGG	TGGCTGTTT	GTATCCTCCT	TTGGCTGATG	CTACTGAGCT	TGGGGCC	1/18 SEQ ID NO. 62
101	G A Q V A V L	Y P P L A D A T E L	TTCATCATCGT	CATGCGCATC	TTGCTAGTCC	TGGGGCC	6/18 SEQ ID NO. 63
96 15mer 2nd.12	GGGGCTTGGC	GTATGTATTT	TTCATCATCGT	CATGCGCATC	TTGCTAGTCC	TGGGGCC	6/18 SEQ ID NO. 64
102	G A W R M Y F	S H R H A H L R S P	TTATGGGGCC				18/18 SEQ ID NO. 65
97: 6mer 2nd.1	GGGGCTCATG	CGGATAGGGT	TTATGGGGCC				18/18 SEQ ID NO. 66
103	G A H A D R V	Y G A					18/18 SEQ ID NO. 67

FIG. 8

COMPARISON OF SIGNALS AT 6.25e11 vir/mL



3RD ROUND ISOLATES

FIG. 9

GENERAL CLONING STRATEGY

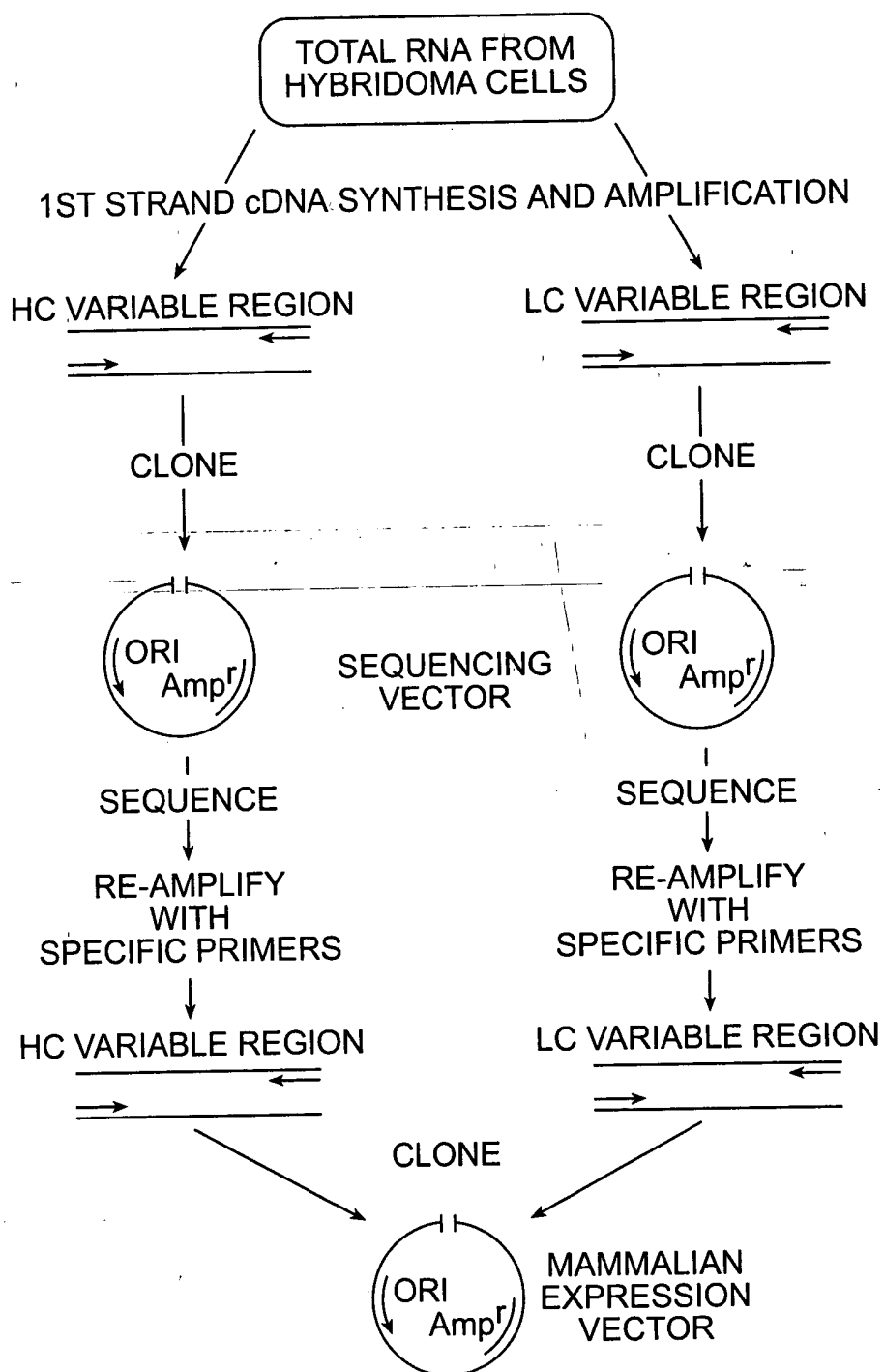


FIG. 10

MOUSE HEAVY CHAIN "FRONT" PRIMERS

JSS1

5'-ATTTCAGGCCCAGCCGGCCATGGCCGARGTRMAGCTKSAKGAGWC-3' SEQ ID NO.68

JSS2

5'-ATTTCAGGCCCAGCCGGCCATGGCCGARGTYCARCTKCARCARYC-3' SEQ ID NO.69

JSS3

5'-ATTTCAGGCCCAGCCGGCCATGGCCAGGTGAAGCTKSTSGARTC-3' SEQ ID NO.70

JSS4

5'-ATTTCAGGCCCAGCCGGCCATGGCCGAVGTGMWGCTKGTGGAGWC-3' SEQ ID NO.71

JSS8

5'-ATTTCAGGCCCAGCCGGCCATGGCCAGGTBCARCTKMARSARTC-3' SEQ ID NO.72

MOUSE HEAVY CHAIN "BACK" PRIMERS

JS160

5'-GCTGCCACCGCCACCTGMRGAGACDGTGASTGARG-3' SEQ ID NO.73

JS161

5'-GCTGCCACCGCCACCTGMRGAGACDGTGASMGTRG-3' SEQ ID NO.74

JS162

5'-GCTGCCACCGCCACCTGMRGAGACDGTGASCARG-3' SEQ ID NO.75

MOUSE LIGHT CHAIN LEADER "FRONT" PRIMERS

PMC12

5'-CCCGGGCCACCATGGAGACAGACACACTCCTG-3' SEQ ID NO.76

PMC13

5'-CCCGGGCCACCATGGATTTTCAAGTGCAGATTTTC-3' SEQ ID NO.77

PMC14

5'-CCCGGGCCACCATGGAGWCACAKWCTCAGGTC-3' SEQ ID NO.78

PMC15

5'-CCCGGGCCACCATGKCCCWRCTCAGYTTCTKG-3' SEQ ID NO.79

PMC55

5'-CCCGGGCACCATGAAGTTGCCTGTTAGGCTG-3' SEQ ID NO.80

MOUSE LIGHT CHAIN "BACK" PRIMER

OKA57

5'-GCACCTCCAGATGTTAACTGCTC-3' SEQ ID NO. 81

"96-110" SPECIFIC PRIMERS

96110HF2

5'-TAATATCGCGACAGCTACAGGTGTCCACTCCCGAAGTGATGCTGGTGGAGWCTG-3' SEQ ID NO.82

96110HB

5'-TTATAGAATTCTTGAGGAGACGGTGAGTGAG-3' SEQ ID NO.83

96110BLF

5'-TTAGGCGATATCGTTCTCTCCAGTCTCC-3' SEQ ID NO.84

96110BLB

5'-GTAACCGTTCGAAAGTGTACTTACGTTTTATTCCAGCATGGTCC-3' SEQ ID NO.85

FIG. 11

96-110 ANTI-STAPH (HAY) HEAVY CHAIN VARIABLE REGION (TYPE IIIA)

GAAGTGATGCTGGTGGAGTCTGGTGAGGATTTGGTGAGCCTAAAGGGTCAATGAACCTCTCATGTGCAGCCTCTGGATTACACCTTCAAT
E V M L V E S G G G L V Q P K G S L K L S C A A S G F T F N

AACTACGCCATGAAT TGGGTCCGCCAGGCTCCAGGAAGGGTTTGGAAATGGGTTGCT
N Y A M N W V R Q A P G K G L E W V A

CGCATAAGAAAGTAAATAATATGCAACATTTTATGCCGATTTCAGTGAAGAC
R I R S K S N N Y A T F Y A D S V K D

AGGTTACCATCTCCAGAGATGATTCACAAAGCATGCTCTATCTGCAATGAACACTTGAAAACTGAGGACACAGCCATGTATTACTGTGTGAGA
R F T I S R D D S Q S M L Y L Q M N N L K T E D T A M Y Y C V R

CGGGGGCTTCAGGGATTGACTATGCTATGGACTAC TGGGTCAAGGAACCTCAGTCACTCCGTCCTCTCA SEQ ID NO. 86
R G A S G I D Y A M D Y W G Q G T S L T V S S SEQ ID NO. 87

96-110 ANTI-STAPH (HAY) LIGHT CHAIN VARIABLE REGION (TYPE VI)

CAAATTGTTCTCTCCAGTCTCCAGCAATCCTGTCTGCATCTCCAGGGAAGGTCAACAATGACTTGC
Q I V L S Q S P A I L S A S P G E K V T M T C

AGGGCCAGCTCAAGTGTAAATTACATGCAC
R A S S S V N Y M H

TGGTACCAGCAGAAGCCAGGATCCTCCCCAAACCCTGGATTCTT GCCACATCCAACCTGGCTTCT
W Y Q Q K P G S S P K P N I S A T S N L A S

GGAGTCCCTGCTCGCTTCAGTGGCAGTGGGTCTGGGACCTCTTACTCTCTCACAATCAGCAGAGTGGAGGCTGAAGATGCTGCCACTTATTACTGC
G V P A R F S G S G S G T S Y S L T I S R V E A E D A A T Y Y C

CAGCAGTGGAGTAGTAAACCACCACG TTCGGAGGGGGACCATGCTGGAATAAGA SEQ ID NO. 88
Q Q W S S N P P T F G G G T M L E I R SEQ ID NO. 89

CDR REGIONS UNDERLINED

FIG. 12

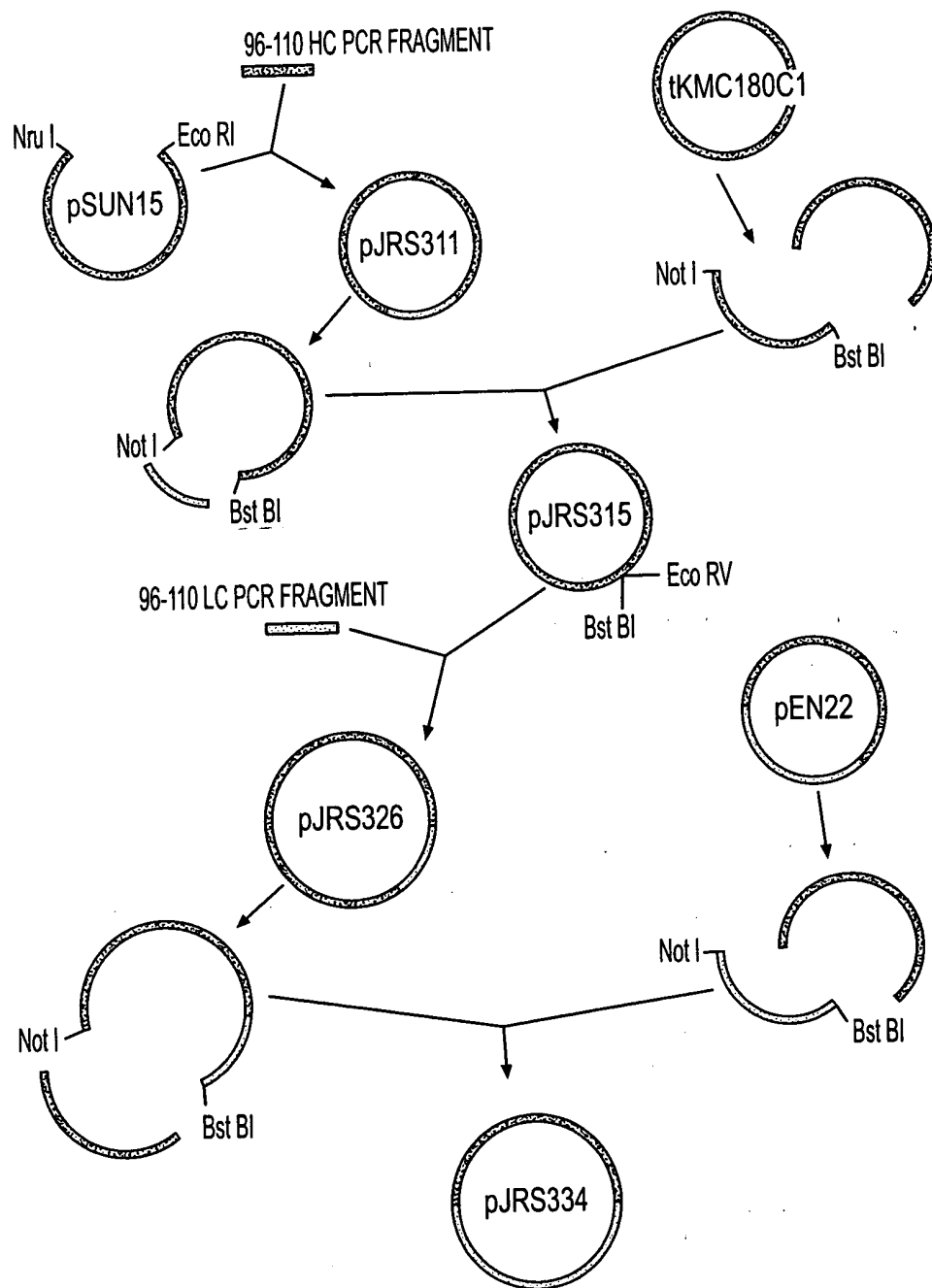
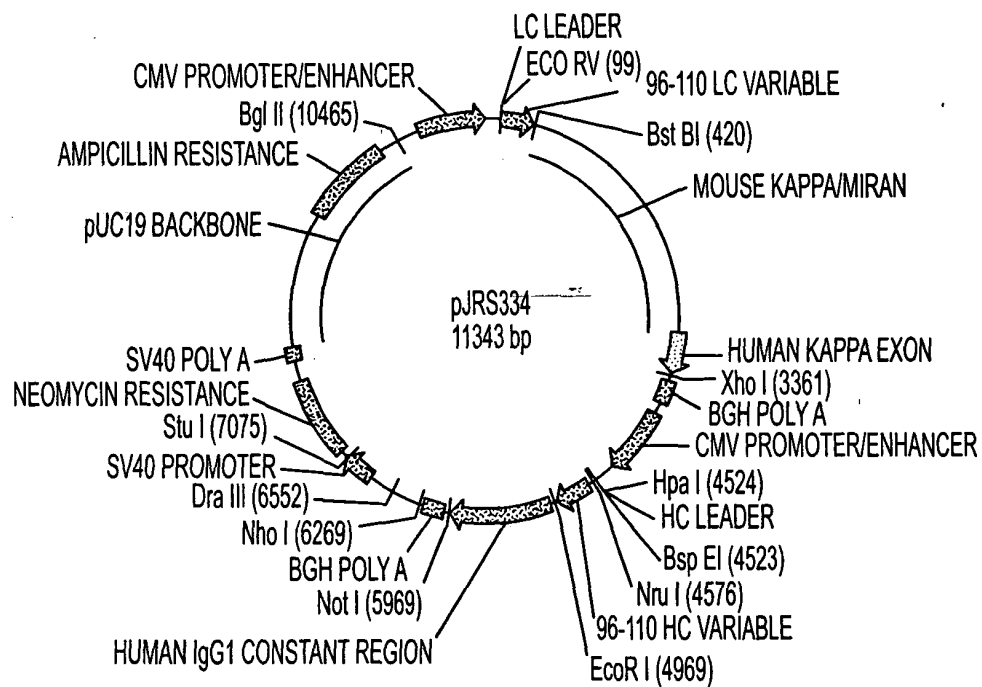


FIG. 13



COMMON UNIQUE RESTRICTION SITES SHOWN

FIG. 14

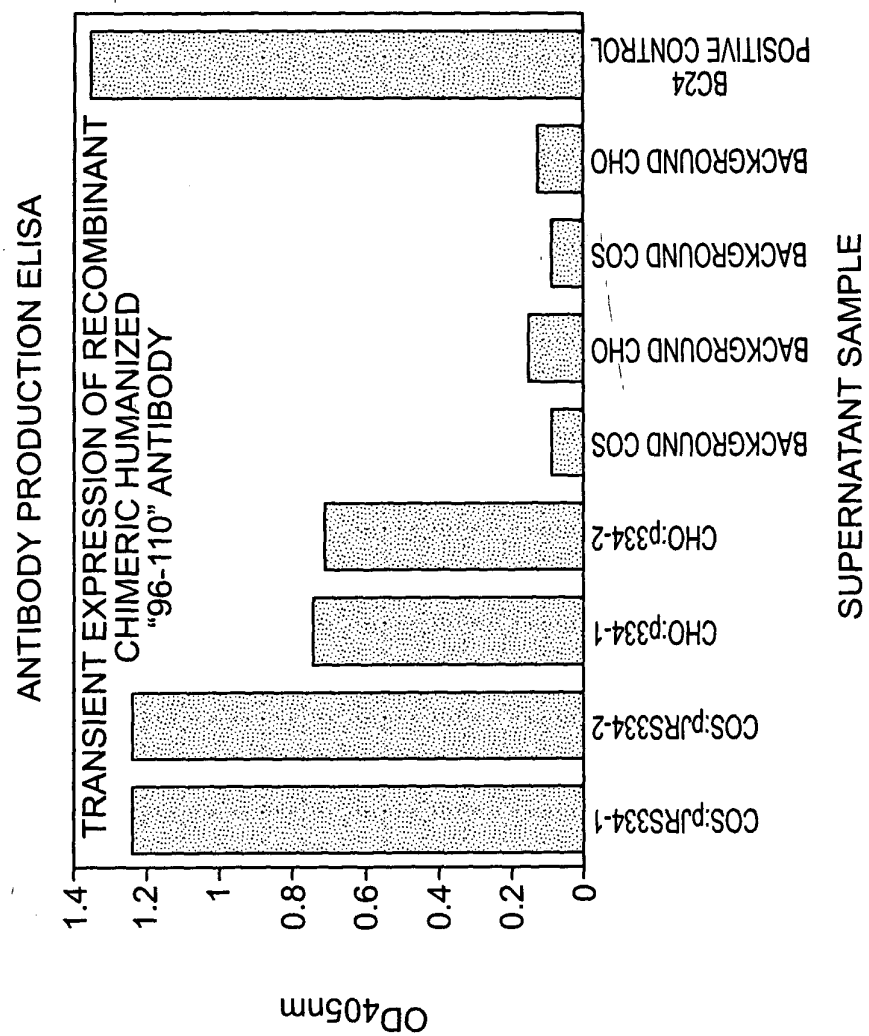


FIG. 15

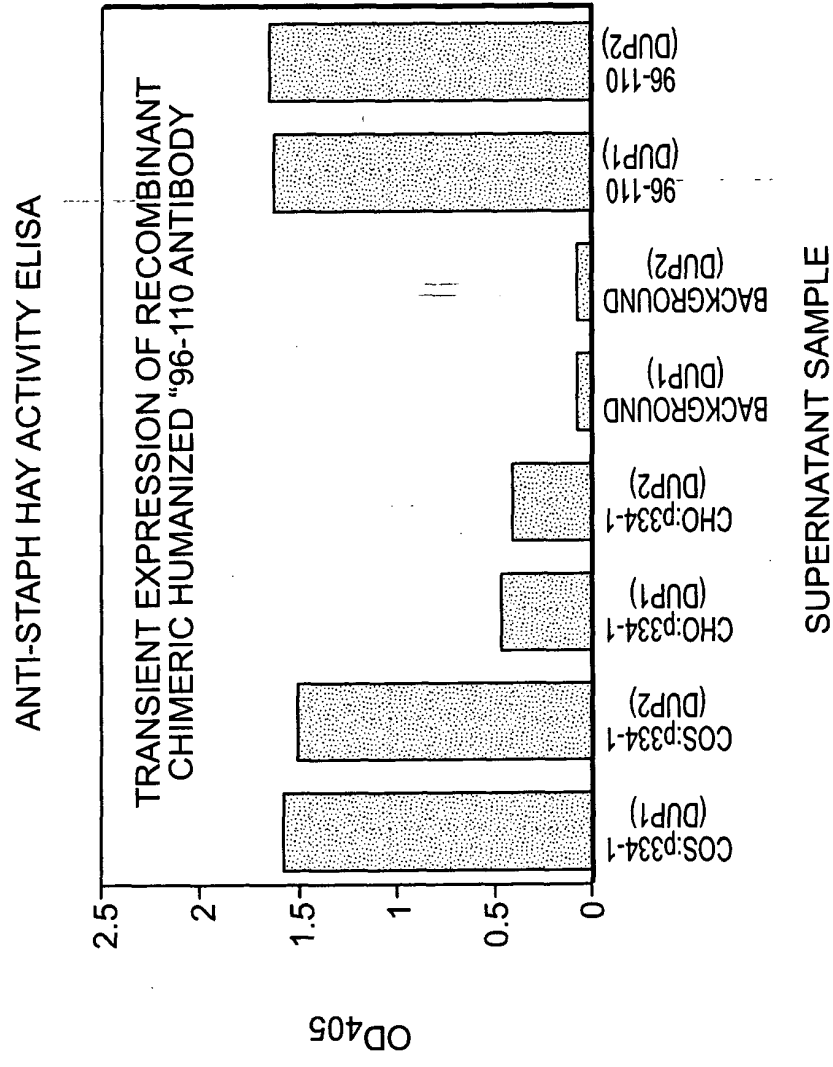
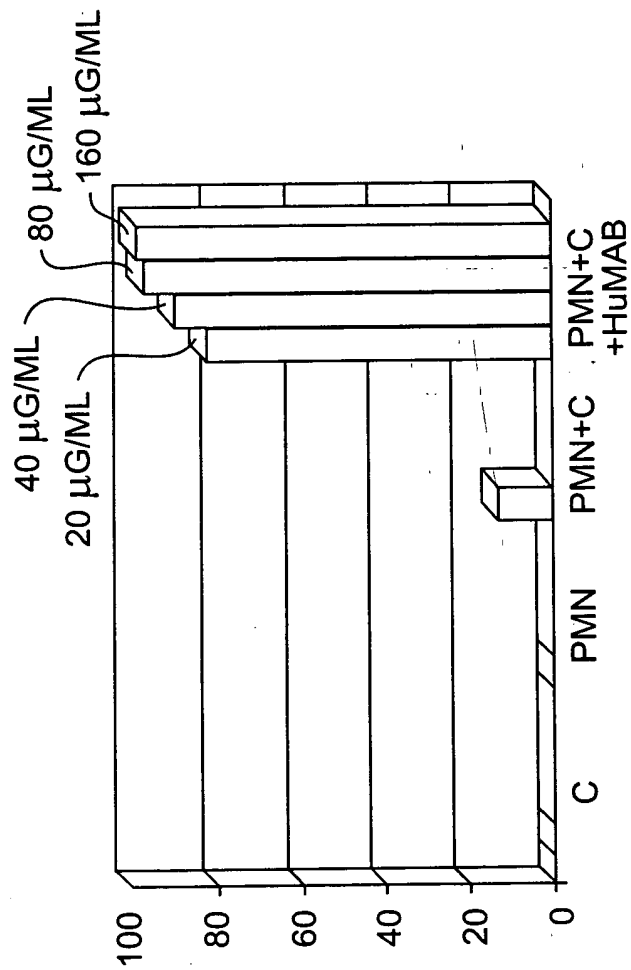


FIG. 16

OPSONIC ACTIVITY OF HuMAB 96-110 FOR S.EPIDERMIDIS
IN A NEUTROPHIL MEDIATED OPSONOPHAGOCYTIC
BACTERICIDAL ASSAY USING HUMAN COMPLEMENT

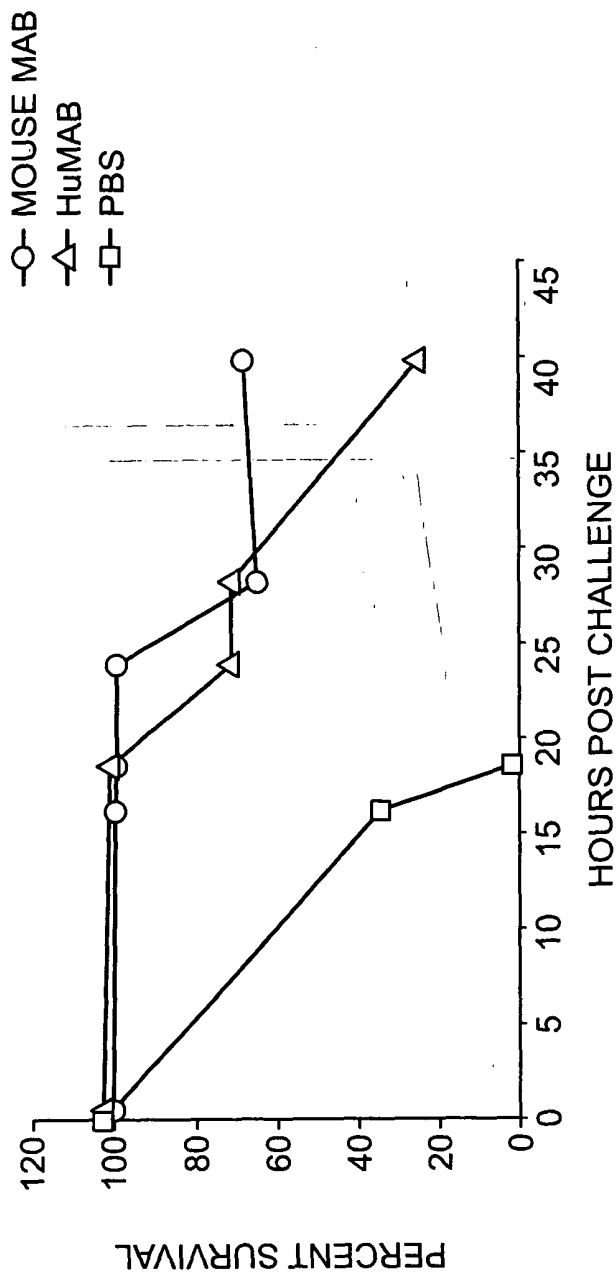
PERCENT BACTERIA KILLED (2HRS)



C- BARB-EX (1:4), HUMAN
PMN-HUMAN
BACTERIA-S.EPIDERMIDIS (STRAIN HAY)

FIG. 17

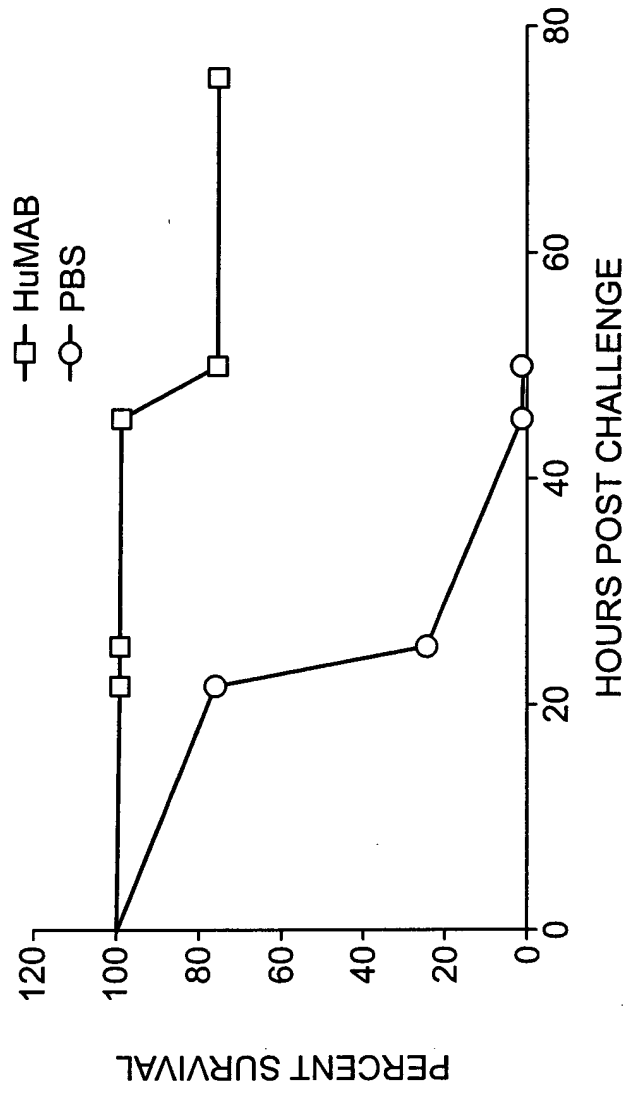
PILOT STUDY TO COMPARE THE EFFECT OF MOUSE
MAB 96-110 AND HuMAB 96-110 IN A LETHAL
MODEL OF S. EPIDERMIDIS SEPSIS



MAB DOSE: 14 mg/kg GIVEN IP, 24 AND 1 HOUR PRIOR TO INFECTION

FIG. 18

SURVIVAL OF CF-1 MICE AFTER INTRAPERITONEAL
CHALLENGE WITH 3×10^9 S. EPIDERMIDIS (HAY)



18 mg/kg/DOSE, IP, 24 AND 1 HOUR PRIOR TO INFECTION

FIG. 19

EFFECT OF HuMAB 96-110 ON BACTEREMIA
IN A LETHAL S. EPIDERMIDIS SEPSIS MODEL

GEOMETRIC MEAN BACTEREMIA LEVEL

SALINE PLACEBO	6.5 x 10 ⁴	7.2 x 10 ⁴	5.2 x 10 ⁴	7 x 10 ³
HuMAB 96-110	3 x 10 ²	7.5 x 10 ²	2.1 x 10 ¹	1.7 x 10 ¹
	4 HRS	8 HRS	12 HRS	18 HRS

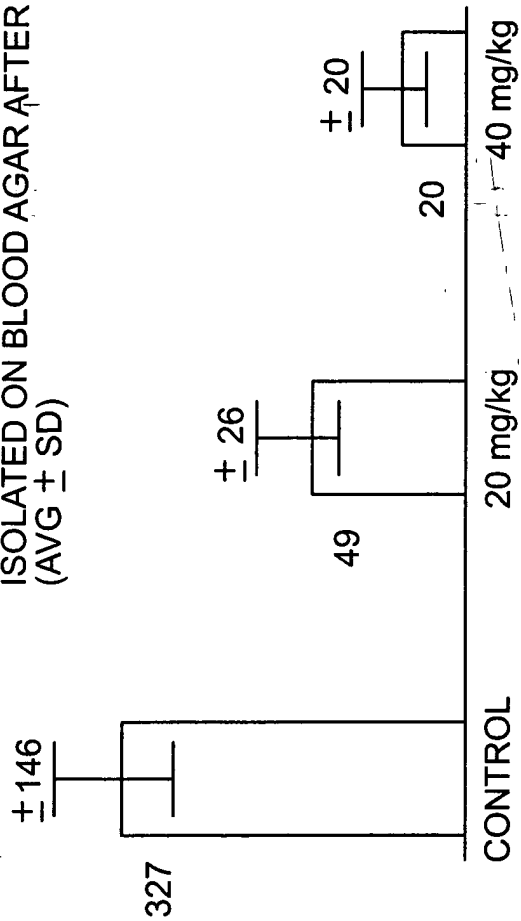
TIME POST INFECTION

HuMAB 96-110 18 mg/kg DOSE OR SALINE GIVEN IP, 24 AND 1 HOUR
PRIOR TO IP INFECTION WITH 3 x 10⁹ S. EPIDERMIDES (HAY)

FIG. 20

BACTEREMIA LEVELS 4 HRS AFTER INFECTION WITH 3×10^9 S.EPIDERMIDIS*

BACTERIA EXPRESSED AS NUMBER OF BACTERIA
ISOLATED ON BLOOD AGAR AFTER 1:1000 DILUTION
(AVG \pm SD)



HuMAB 96-110/DOSE

* CF-1 MICE INFECTED IP WITH STRAIN HAY-HuMAB GIVEN IP x 2

FIG. 21

THE EFFECT OF Hu 96-110 ON SURVIVAL IN A LETHAL
NEONATAL S.EPIDERMIDIS* SEPSIS MODEL: STUDY II

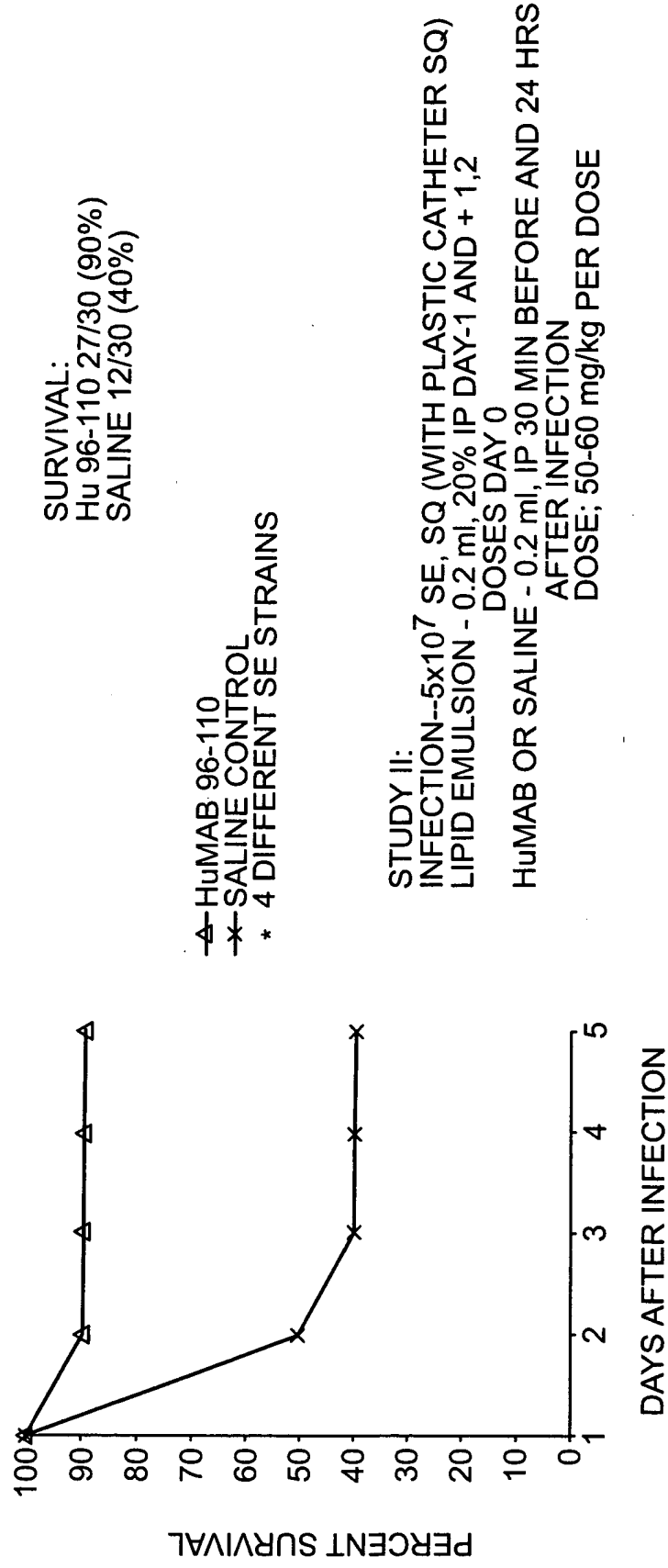


FIG. 22